DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

FOI

TRANSMITTED VIA FACSIMILE

NOV 25 1998

Eloise R. Scott, D.V.M.
Associate Director
U.S. Regulatory Affairs
SmithKline Beecham Pharmaceuticals
1250 South Collegeville Road
PO Box 5089
Collegeville, PA 19426-0989

RE: NDA 20-489
Androderm (testosterone transdermal system)
MACMIS ID #7324

Dear Dr. Scott:

As part of its routine monitoring and surveillance program, the Division of Drug Marketing, Advertising, and Communications has become aware of the following promotional materials for Androderm (testosterone transdermal system), disseminated by SmithKline Beecham Pharmaceuticals (SKB), that are in violation of the Federal Food, Drug, and Cosmetic Act and its implementing regulations.

"Make the Call!" leaflet (AD8706)

This leaflet, submitted on Form FDA 2253 to DDMAC on September 11, 1998, contains the following misleading claims:

"*Patients prefer* **Androderm** *over* **Testoderm TTS.**"

"In a *Testoderm TTS* clinical trial, when questioned about product preference, patients reported they felt *Androderm was a better treatment than Testoderm TTS* in terms of effectiveness, side effects, convenience and wearing comfort."

These claims are misleading because they suggest that patients prefer Androderm over Testoderm TTS and that Androderm is superior to Testoderm in terms of effectiveness, side effects, convenience, and wearing comfort, and delivery system when such has not been demonstrated by substantial evidence. The evidence cited in support of this claim represents data from an open label study, utilizing a non-validated measure, that does not support comparative claims. DDMAC is unaware of substantial evidence, in the form of controlled, head-to-head

clinical trials comparing Testoderm TTS and Androderm, that supports these superiority claims and representations.

"*Clinical trials indicate* **Androderm** *produces higher serum testosterone concentrations than* **Testoderm TTS.**"

This claim and corresponding graphic presentation, based on a side by side comparison of the approved product labeling (PI) for each product, are misleading because they suggest that Androderm is clinically superior to Testoderm TTS based on serum testosterone concentrations when such has not been demonstrated by substantial evidence. It should be noted that both products maintain testosterone levels in the normal physiologic range, which is the key efficacy parameter used in evaluating testosterone replacement therapies.

"**Androderm**...*the only testosterone transdermal system with an advanced adhesion system that avoids the difficulties associated with patch detachment*"

This claim, and related representations, is misleading because it suggests that Androderm is superior to Testoderm TTS in terms of patch detachment when such has not been demonstrated by adequate evidence.

"Only *Androderm* has the advantage of patient wear during sex, showering or exercising..."

This claim is misleading because it suggests that Androderm is the only testosterone transdermal system that may be worn during sex, showering, or exercising. The patient package insert (PPI) for Testoderm TTS clearly states that the patch may be worn during sex. Furthermore, neither the PI or PPI for Testoderm TTS prohibit wearing the patch during showering, bathing, or exercise.

Promotional Dear Doctor Letter (AD9590)

This letter, submitted on Form FDA 2253 to DDMAC on August 14, 1998, is misleading because it suggests that Androderm is safe and effective for treating non-insulin dependent diabetes mellitus (NIDDM) when such has not been demonstrated by adequate and well-controlled clinical trials. The letter, written on SKB letterhead and signed by SKB representatives, makes the following statements and representations about the use of Androderm in patients with NIDDM:

"I would like to share new clinical data that may be of importance to you and your male patients with non-insulin dependent diabetes mellitus (NIDDM)."

"An association has been found between diabetes and hypogonadism in several studies..."

"Data from several studies indicate that there is an optimal range for testosterone levels and that too low too high testosterone levels may be associated with insulin resistance."

"The finding of greatest importance was that testosterone supplementation to achieve normal testosterone concentrations may result in significant improvements in insulin sensitivity, thereby potentially improving glucose control...."

Androderm is indicated for testosterone replacement in men for conditions associated with a deficiency or absence of endogenous testosterone. SKB has not provided adequate evidence that would support claims or representations that Androderm therapy improves insulin sensitivity or glucose control in patients with NIDDM.

In order to address this objection, DDMAC requests that SKB take prompt action to correct the violations discussed in this letter and prevent their recurrence. DDMAC requests that these actions include:

1. The immediate cessation of dissemination of all promotional activities and materials that contain the same or similar violations.

2. Provide to DDMAC, in writing, SKB's intent to comply with #1 above. Your response should be received by December 10, 1998.

3. This response should include a list of all similarly violative promotional materials and SKB's method for discontinuing their use.

If SKB has any questions or comments, please contact the undersigned by facsimile at (301) 594-6771, or at the Food and Drug Administration, Division of Drug Marketing, Advertising and Communications, HFD-40, Rm 17B-20, 5600 Fishers Lane, Rockville, MD 20857. DDMAC reminds SKB that only written communications are considered official.

In all future correspondence regarding this particular matter, please refer to MACMIS ID #7324 in addition to the NDA number.

Sincerely,

Mark W. Askine, R.Ph.
Regulatory Review Officer
Division of Drug Marketing,
Advertising and Communications